REMARKS

Formal Matters:

Claims 24-30 are pending in the application.

Claim 27 is amended to add a recitation that was previously omitted as an inadvertent typographical error. Support for recitation of a neurological disorder is found throughout the specification such as at, for example, page 2, lines 30-31.

Claims 29 and 30 are amended to recite the correct claim dependency. Claims 29 and 30 were intended to depend from claim 28 and due to an inadvertent typographical error, they were made dependent from claim 27. Applicants have amended claims 29 and 30 to depend from claim 28.

No new matter is added by the amendments and the Examiner is respectfully requested to enter them.

Priority:

The priority claimed for the present application is amended in paragraph 1, page 1 to indicate that the present application is a continuation of U.S. Application Serial No. 09/234,730, filed January 21, 1999, etc. Applicants point out that this priority information was provided in the transmittal letter submitted upon the filing of the present application (August 25, 2000). Thus, the amendment to the priority data adds no new matter.

Claim Rejections:

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 27, 29, and 30 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite because claim 27 is incomplete for not referring to a pathological condition. Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

Claim 27 is amended to recite "a neurological disorder" as the pathological condition due to absence of the CT-1 polypeptide. As noted, supra, support for the amendment is found on page 2, lines 30-31.

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Applicants submit that the rejection is overcome. Withdrawal of the rejection and allowance of the claim is respectfully requested.

Claims 29 and 30, previously dependent from claim 27 have been amended to depend from claim 28 for the reasons provided *supra*. The rejection under Section 112, second paragraph is moot. Withdrawal of the rejection and allowance of the claims is respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 24-30 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly non-enabling for a non-human animal comprising homologously recombined DNA wherein the CT-1 gene of the animal is altered such that the CT-1 polypeptide of the animal is defective or absent. Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

Applicants disclose procedures for generating knock-out animals constructed to have a defective or altered gene encoding a CT-1 polypeptide as a result of homologous recombination between the endogenous gene encoding the CT-1 polypeptide and altered genomic DNA encoding the same polypeptide introduced into an embryonic cell of the animal (see page 26, lines 9-26 of the specification).

The ability to construct such animals is shown by Oppenheim, R.W. et al. (Journal of Neuroscience, 21(4):1283-1291 (2001)(The on-line version of the article is enclosed. The tables and figures are enlarged for the convenience of the Examiner.). Viable *ct-1* knock-out mice and viable *ct-1* heterozygotes were constructed as disclosed in the Materials and Methods section by homologous recombination of the CT-1 gene in embryonic stem (ES) cells. Mice with homologous recombination of the *ct-1* gene were obtained by established techniques (see page 3, third paragraph of the article). The recombination of the *ct-1* gene resulted in a deletion

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of a region spanning exon 2 and the complete coding region of exon 3 (see Fig. 3). Heterozygous embryonic stem cell clones were identified and viable heterozygous mice carrying the mutation were generated by standard knock-out techniques. Back-crossing of the heterozygotes provided viable *ct-1* -/- and *ct-1* +/+ mice (see page 7, last paragraph to page 8 of the article). *In situ* hybridization of tissue from wild-type and *ct-1* -/- mice using probes specific for the intact and deleted regions of the recombination showed that CT-1 mRNA was not expressed in the KO mice, indicating that CT-1 polypeptide was not produced in the KO mice. (see Fig. 3 of Oppenheim et al.)

As a result of these showings, the construction of non-human KO animals in unpredictable is moot with respect to the claimed non-human animals wherein the CT-1 gene of the animal is altered such that CT-1 polypeptide of the animal is defective or absent was enabled by Applicants' specification. Withdrawal of the rejection under section 112, first paragraph and allowance of the claims is respectfully requested.

SUMMARY

Claims 24-30 are pending in the application.

Claim 27 has been amended to add a recitation previously omitted by inadvertant typographical error, thereby overcoming the rejection under 35 U.S.C. § 112, second paragraph.

The rejection under 35 U.S.C. § 112, first paragraph has been overcome by pointing out that the preparation of a CT-1 knock-out animal as disclosed in the specification was accomplished, thereby showing that the specification was enabling. A copy of Oppenheim et al. is enclosed herewith.

The rejections of the claims have been overcome and the claims are in condition for allowance, which action is respectfully requested.

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If the Examiner believes that an interview would be helpful to expedite prosecution, the Examiner is invited to contact the undersigned attorney at (650) 225-2066.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

This document is submitted with a transmittal and a petition for a three-month extension of time and fees. In the unlikely event that any of these documents is separated from this document, Applicants hereby petition the Commissioner to authorize charging our Deposit Account 07-0630 for any fees required or credits due and to apply any extensions of time necessary to maintain the pendency of this application.

Respectfully submitted,
GENENTECH, INC.

Date: June 22, 2001

By: _____
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Doc # 86557

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Version with markings to show changes made

In the specification:

Please amend the specification on page 1, paragraph 1 under "Cross-Reference to Related Applications" to read as follows:

This is a non-provisional continuation application filed under 37 C.F.R. 1.53(b)(1), claiming priority under 35 U.S.C. 120 to U.S. Application Serial No. 09/234,730 filed January 21, 1999, which is a continuation U.S. Application Serial No. 09/033,114 filed March 2, 1998, which is a continuation of U.S. Application Serial No. 08/733,850 filed October 18, 1996, now abandoned, which is a continuation of U.S. Application Serial No. 08/443,129 filed May 17, 1995, issued May 6, 1997 as U.S. Patent No. 5,627,073, which is a divisional application of 08/286,304 filed August 5, 1994, issued November 5, 1996 as U.S. Patent No. 5,571,893, which is a continuation-in-part of U.S. Application Serial No. 08/233,609 filed April 25, 1994, issued July 9, 1996 as U.S. Patent No. 5,534,615, and to U.S. Application Serial No. 60/113,296, filed December 22, 1998, now abandoned, which applications are herein incorporated by reference in their entirety.

Claims 27, 29 and 30 have been amended as follows:

27. (Amended) The animal of claim 25 wherein the pathological condition is a neurological disorder.

29. (Amended) The animal of claim ~~27~~ 28 wherein the animal is a mouse.

30 (Amended) The animal of claim ~~27~~ 28 wherein the animal is a rat.

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